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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/121,239	07/23/1998	RICHARD C. HARVEY	GP091-02.UT	3098

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EXAMINER	
SCHMIDT, MARY M	

ART UNIT	PAPER NUMBER
1635	29

DATE MAILED: 09/10/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/121,239	Applicant(s) HARVEY ET AL.	
	Examiner Mary Schmidt	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 June 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *26*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Specification

1. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 since the brief description of the drawings (Figures 2 and 3) on page 13 of the specification does not reference the sequences in the figures by SEQ ID NO. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) before the application can be examined under 35 U.S.C. §§ 131 and 132.

2. The abstract of the disclosure is objected to because it is less than 50 words. Correction is required. See MPEP § 608.01(b).

3. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

Claim Rejections - 35 USC § 112

4.The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 21-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

New claim 21 is drawn to a method of detecting a fusion mRNA transcript produced as a result of a human bcr-abl translocation comprising the steps of: (a) providing a sample containing a human fusion mRNA transcript comprising a bcr-abl splice junction; (b) contacting under isothermal nucleic acid amplification conditions: the fusion mRNA transcript, a first primer which hybridizes to the/a second primer which hybridizes to the complement of the fusion mRNA transcript at a primer binding site derived from a bcr region flanking the bcr-abl splice junction site, a second primer which hybridizes to the complement of the fusion mRNA transcript at a primer binding site derived from a bcr region flanking the bcr-abl splice junction site, at least one enzyme having an RNA-directed DNA polymerase activity, and at least one

enzyme having an DNA-directed RNA polymerase activity; c) amplifying the fusion mRNA transcript in a single nucleic acid amplification reaction that uses the first primer to produce a second strand complementary to at least a portion of the fusion mRNA transcript containing the bcr-abl splice junction site, the second primer to produce a third nucleic acid strand of the same sense as the fusion mRNA transcript containing the bcr-abl splice junction site, and the DNA-dependent RNA polymerase activity to produce amplified RNA that is complementary to the fusion mRNA transcript comprising the bcr-abl splice junction; (d) hybridizing the amplified RNA with an oligonucleotide probe which hybridizes to a probe binding site derived from a bcr region flanking the bcr-able splice junction, thereby forming a hybridization complex; and (e) detecting the hybridization complex as an indication of the presence of the fusion mRNA transcript in the sample. The claim contains 7 a typographical error in line 7, which claims "a first primer which hybridizes to *the a* second primer." Furthermore, the claim does not clearly explain the metes and bounds of the primers since based on the teachings of the specification (such as Example 2, page 13) the structure of the first primer that hybridizes to the second primer is unclear. The specification as filed teaches that the primers are on either side of the bcr/abl junction, and thus do not hybridize to each other. Furthermore, it is not clear how the primers of claims 23-26 act according with these limitations since primers of SEQ ID NOS: 1 and 5 appear to bind to opposite sides of the bcr/abl junction, and thus do not hybridize to one another. Clarification is required.

6. Claims 21-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

See the description of new claim 21 above. Applicant states on page 9 of the response filed 6/21/02, that "[s]upport for the amendments is provided throughout the disclosure as described below and in Figures 1A to 1C, Figures 2 and 3, page 12, line 15 to page 13, line 15, page 19, line 25 to page 22, line 6, and Examples 2 to6 9page 27, line 25 to page 35, line 8). However, no where in this description does Applicant specifically point out the new limitations of claims 21 and 22 and the use of the primers in claims 23-26, as pointed out above, do not appear to correlate to the claimed steps (esp. the "contacting" step (b) of claim 21).

MPEP 2163 teaches the following conditions for the analysis of the claimed invention at the time the invention was made in view of the teachings of the specification and level of skill in the art at the time the invention was made:

> **The claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence....A lack of written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process....Generally, there is an inverse correlation between the level of skill**

and knowledge in the art and the specificity of disclosure necessary to satisfy the written description requirement....The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

In the instant case, absent a specific teaching the specification as filed of the new claimed method steps, one of skill in the art would not have been able to immediately envisage the claimed primer structures based solely on the functional language of amplifying the bcr/abl translocation. As argued above, the disclosed primer sequences did not hybridize to each other, and so it is not clear from the specification as filed, what the structure of the new primers of claims 21-22 are. Without further explanation of the direct support in the specification, one of skill in the art would not have recognized the primers of the new claims 21-22 sufficient to show that Applicant was in possession of the claimed genus of new primers and that new matter was not introduced to the specification as filed. The ambiguity of the language of the new claims precludes a clear picture of the claimed invention, the apparent meaning of which appears to lack written description support in the specification as filed.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-5 and 9-17 stand rejected under 35 U.S.C. 102(b) as being anticipated by Sooknanan et al. (Experimental Hematology 21:1719-1724, 1993) for the same reasons of record as set forth in the Official Action mailed 12/21/01.

Applicant's arguments filed 6/21/02 have been fully considered but they are not persuasive.

Applicant argues on page 12 and 13 of the response that Sooknanan et al. teach nested primers that overlap the bcr/abl junction and therefore do not meet the description of Applicant's invention as taught on page 17, lines 20-21, page 18, lines 23-24, page 19, lines 1-6, page 19, lines 22-24 or page 19, line 29 through page 30, line 3.

Applicant is reminded of the teachings of MPEP 2111.01 which states that "[w]hile the meaning of claims of issued patents are interpreted in light of the specification, prosecution history, prior art and other claims, this is not the mode of claim interpretation to be applied terms reasonably allow." The instant claims are drawn to method steps that are "consisting essentially of" the recited steps. MPEP 2111.03 states that "[t]he transitional phrase "consisting

essentially of" limits the scope of a claim to the specified materials or steps "and those that do not materially affect the basic and novel characteristic(s)" of the claimed invention.... "A 'consisting essentially of' claim occupies a middle ground between closed claims that are written in a 'consisting of' format and fully open claims that are drafted in a 'comprising' format."..."absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising."..."If an applicant contends that additional steps or materials in the prior art are excluded by the recitation of "consisting essentially of," applicant has the burden of showing that the introduction of additional steps or components would materially change the characteristics of applicant's invention."

In the instant case the claims are interpreted to be anticipated by the teachings of Sooknanan et al. since the claims do not specifically claim reactions with only one set of primers and Applicant's disclosure as a whole of the invention does not necessarily limit the invention to use of one set of primers only. Just because the optimal embodiment in the specification as filed "does not require use of serial amplification reactions" does not completely limit the "reasonable" breath of the claimed invention to methods having only one set of amplification primers. The burden is on Applicant according to MPEP 2111.03 to show how the use of the primers taught by Sooknanan et al. is considered to "materially affect the basic and novel characteristic(s)" of the instantly claimed invention to amplification of any fusion nucleic acid "consisting essentially of" the claimed method steps. Since Sooknanan et al. teaches methods

that have the basic characteristics of the instantly claimed steps, ie. detection and amplification of fusion nucleic acids, specifically the bcr/abl fusion nucleic acid, Applicant has not demonstrated that the claims as written can not reasonably embrace the teachings of Sooknanan et al. Therefore, the addition of the limitation "single" isothermic reaction, is not interpreted to exclude other steps from the claimed methods. Similarly, the probes used by Sooknanan et al. are considered embraced by the "consisting essentially of" language since such language renders the claim limitations open, and the burden is on Applicant to teach why the probes used in Sooknanan et al. "materially affect the basic and novel characteristic(s)" of the claimed method of detection of the amplified bcr/abl fusion product especially in view of the fact that the probes used by Sooknanan et al. would have detected the t(9;22) bcr/abl fusion products, the same invention disclosed by Applicant. Furthermore, Applicant's invention according to Figure 1C, embraces an abl probe that spans the translocation junction, and page 19 of the specification states that "[t]he probes may be targeted to any region of the amplified nucleic acid, so long as the probe is capable of hybridizing to the amplified nucleic acid." Therefore, the embodiments taught by Sooknanan were specifically described in the specification as filed and would therefore be considered reasonably embraced by the "consisting essentially of" language of the claimed as instantly written in view of Applicant's disclosure of the claimed invention.

9. Claims 19 and 20 stand rejected under 35 U.S.C. 102(a) as being anticipated by Qiagen Oligotex Direct Protocol for isolation of PolyA+ mRNA from cytoplasm of cultured cells (reference in Qiagen product guide, 1/98, page 61 and protocol from Qiagen web page www.qiagen.com) for the same reasons of record as set forth in the Official Action mailed 12/21/01.

Applicant's arguments filed 6/21/02 have been fully considered but they are not persuasive.

Applicants point out the instant invention has priority to the provisional application 60/053,509, dated July 23, 1997. Applicant's argue that the date of the Qiagen product guide is not prior to Applicant' invention and thus is not prior art. However, the Qiagen Oligotex mRNA protocol was available to one skilled in the art prior to Applicants priority date. Although the date of the Internet reference cited is after the filing date, the prior art taught that it was used prior to Applicant's filing. The Examiner did not have access to the original publication of the Oligotex protocol, and thus necessarily reproduced it from a later catalog. However, both U.S. Patents 5,837, 493 (priority to Jan. 1997) and 6,054,294 (priority to Feb. 1997) teach that the Oligotex protocol was known: see section 144 of the '294 patent that states that "Qiagen's Oligotex mRNA isolation system was used as described by the manufacturer; the procedure was repeated twice to obtain pure poly (a). Sup.+ RNA."; see sections 156 and 160 of the '493 patent that state that "the RNA was isolated using the Qiagen Oligotex kit (Qiagen Inc., Chatsworth Calif.).... the poly (A+) RNA was isolated using the Qiagen Oligotex kit (Qiagen Inc.)...."

Absent evidence to the contrary, the buffers and directions for mRNA isolation were the same in the protocol provided to Applicant and the methods described in U.S. Patents '493 and '294.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 6-8 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Sooknanan et al. in view of Qiagen Oligotex Direct protocol for isolation of Poly A+ mRNA as set forth above for the same reasons of record as set forth in the Official Action mailed 12/21/01.

Applicant's arguments filed 6/21/02 have been fully considered but they are not persuasive.

Applicant argues all the same arguments encountered above in regards to the teachings of Sooknanan et al. and the priority date of the Qiagen Oligotex protocol. As argued above, the teachings of Sooknanan et al. are embraced by the claims given their broadest reasonable interpretation. Furthermore, the teachings of the Qiagen protocol were art recognized prior to Applicant's priority date.

12. Claims 18 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Sooknanan et al. in view of Qiagen Oligotex Direct protocol for isolation of Poly A+ mRNA as set forth above and further in view of Burg et al. (U.S. Patent 6,300,068 B1) for the same reasons of record as set forth in the Official Action mailed 12/21/01.

Applicant's arguments filed 6/21/02 have been fully considered but they are not persuasive.

Applicant argues all the same arguments encountered above in regards to the teachings of Sooknanan et al. and the priority date of the Qiagen Oligotex protocol. As argued above, the teachings of Sooknanan et al. are embraced by the claims given their broadest reasonable interpretation. Furthermore, the teachings of the Qiagen protocol were art recognized prior to Applicant's priority date.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to *Mary M. Schmidt*, whose telephone number is (703) 308-4471.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *John LeGuyader*, may be reached at (703) 308-0447.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group Analyst, *Kay Pinkney*, whose telephone number is (703) 305-3553.

M. M. Schmidt
September 8, 2002

SEAN McGARRY
PRIMARY EXAMINER
1635